

SEP 7 - 2007

PATENT  
Docket No. 265.0045 0101IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Hamill et al. )  
Serial No.: 10/585,503 )  
Confirmation No.: 2236 )  
Filed: 17 January 2007 )  
For: MECHANOSENSITIVE ION CHANNELS AND METHODS OF USE

Group Art Unit: 1642  
Examiner: Unknown

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September 7, 2007  
Date

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PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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For: MECHANOSENSITIVE ION CHANNELS AND METHODS OF USE  
Patent Application Publication No.: US 2007/0190600 A1

REQUEST FOR CORRECTION OF PATENT APPLICATION PUBLICATION

Mail Stop PGPUB  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

This paper is a request for correction and republication of the above-identified Patent Application Publication, which was published on 16 August 2007.

Applicant's Representatives identified the following errors made by the U.S. Patent and Trademark Office: typographical errors. The errors are indicated on the form entitled "Errors on Published Application" included herewith.

Pursuant to 37 C.F.R. §1.221(b), we request that the error(s) indicated above be corrected, and that the above-identified Patent Application Publication be re-published without additional publication or processing fees.

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Errors on Published ApplicationInventor: Hamill et al.Filed: 17 January 2007Proofreader's Initials: dnmFile No. 265.0045 0101Serial No. 10/585.503Confirmation No. 2236Application Publication Date: 16 August 2007

Published Application Page/Col.	Line #	Application as Filed		Error Fault	Correction
		Page	Line #		
Face page		Application Data Sheet		PTO	Inventor Marato should be Maroto
Page 23, Col. 1 (claim 12)	14	48	14	PTO	decrease should be decreases
Page 23, Col. 1 (claim 14)	21	48	21	PTO	polypeptides should be polypeptide
Page 23, Col. 1 (claim 19)	30	48	34	PTO	identifies should be identified
Page 23, Col. 1 (claim 21)	41	49	2	PTO	After "amount" insert -of a composition comprising an agent that decreases activity of a-
Page 23, Col. 1 (claim 25)	56	49	24	PTO	After "comprising SEQ ID NO:" insert -   -.
Page 23, Col. 1 (claim 25)	56	49	24	PTO	Delete "to"
Page 23, Col. 1 (claim 26)	57	49	26	PTO	Delete "The method of claim 24 wherein the agent is a polypeptide comprising SEQ ID NO: 1 or SEQ ID NO:7." and insert -The method of claim 23 wherein the agent is an antibody that specifically binds an MscCa polypeptide.-
Page 23, Col. 2 (claim 31)	27	50	22	PTO	RNS should be RNA
Page 23, Col. 2 (claim 32)	33	50	27	PTO	comprise should be comprises



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(19) **United States**(12) **Patent Application Publication**  
**Hamill et al.**(10) **Pub. No.: US 2007/0190600 A1**(43) **Pub. Date: Aug. 16, 2007**(54) **MECHANOSENSITIVE ION CHANNELS AND  
METHODS OF USE****Related U.S. Application Data**(60) Provisional application No. 60/535,327, filed on Jan.  
9, 2004.(75) Inventors: **Owen P. Hamill, Galveston, TX (US);**  
**Rosario Marato, Galveston, TX (US)****Publication Classification**Correspondence Address:  
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**P.O. BOX 581415**  
**MINNEAPOLIS, MN 55458 (US)**(51) **Int. Cl.**  
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(52) **U.S. Cl.** ..... **435/69.1; 435/320.1; 435/325;**  
**530/350; 536/23.5**(73) Assignee: **Board of Regents, The University of  
Texas System, Austin, TX (US)**(57) **ABSTRACT**(21) Appl. No.: **10/585,503**  
(22) PCT Filed: **Jan. 10, 2005**  
(86) PCT No.: **PCT/US05/00722**  
**§ 371(c)(1).**  
(2), (4) Date: **Jan. 17, 2007**

The present invention provides methods for identifying agents that decrease the activity of a mechanosensitive ion channels, preferably, a mechanosensitive  $Ca^{2+}$ -permeable channel (MscCa) channel. The present invention also provides methods for using agents that decrease the activity of mechanosensitive ion channels, including, for instance, methods for treating cancer, methods for decreasing metastasis of a cancer cell, and methods for decreasing a symptom associated with cancer.

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Aug. 16, 2007

23

11. An agent identified by the method of claim 1.  
 12. A method for identifying an agent that decreases a phenotype of a cell comprising:

contacting a cell expressing an MscCa channel with a candidate agent to yield a treated cell; and

comparing the phenotype of the treated cell with the phenotype of a control cell not contacted with the candidate agent, wherein the phenotype is selected from the group of motility, invasiveness, proliferation, and a combination thereof, and wherein a decreased phenotype for the treated cell indicates the candidate agent decreases the phenotype.

13. The method of claim 12 wherein the candidate agent causes activity of an MscCa channel of the treated cell to decrease.

14. The method of claim 12 wherein the MscCa channel comprises a polypeptide comprising an amino acid sequence of at least 90% identity to SEQ ID NO: 2, wherein the polypeptide has MscCa activity.

15. The method of claim 14 wherein the MscCa channel comprises a polypeptide comprising SEQ ID NO: 2.

16. The method of claim 12 wherein the cell is a tumor cell.

17. The method of claim 12 wherein the cell is a human prostate tumor cell line.

18. The method of claim 17 wherein the human prostate tumor cell line is ATCC CRL-1435.

19. An agent identified by the method of claim 12.

20. A method for treating cancer comprising:

administering to a subject having cancer an effective amount of a composition comprising an agent that decreases activity of a mechanosensitive ion channel present on a cancer cell, wherein a symptom of the cancer is decreased.

21. A method for decreasing metastasis of a cancer cell comprising:

administering to a subject at risk of developing cancer an effective amount of a mechanosensitive ion channel.

22. A method for decreasing a symptom associated with cancer comprising:

administering to a subject having cancer an effective amount of a composition comprising an agent that decreases activity of a mechanosensitive ion channel.

23. The method of claim 20, 21, or 22 wherein the mechanosensitive ion channel is a mechanosensitive  $Ca^{2+}$ -permeable (MscCa) channel.

24. The method of claim 20, 21, or 22 wherein the agent is a polypeptide comprising an amino acid sequence comprising at least 90% identity to SEQ ID NO: 1 or to SEQ ID NO: 7.

25. The method of claim 24 wherein the agent is a polypeptide comprising SEQ ID NO: 1 or SEQ ID NO: 7.

26. The method of claim 24 wherein the agent is a polypeptide comprising SEQ ID NO: 1 or SEQ ID NO: 7.

27. The method of claim 26 wherein the antibody binds to an epitope present on SEQ ID NO: 5 or SEQ ID NO: 6.

28. The method of claim 23 wherein the MscCa channel comprises an MscCa polypeptide, and wherein the agent is a polynucleotide that decreases expression of the MscCa polypeptide.

29. The method of claim 20, 21, or 22 wherein the cancer is prostate cancer, breast cancer, colon cancer, lung cancer, bladder cancer, ovary cancer, pancreas cancer, or skin cancer.

30. The method of claim 23 wherein the agent decreases activity of an MscCa channel comprising a polypeptide comprising SEQ ID NO: 2.

31. A method for inhibiting expression of an MscCa polypeptide comprising:

administering into a cell an effective amount of an RNA polynucleotide, wherein the polynucleotide comprises a sense strand and an antisense strand, wherein the sense strand comprises a nucleotide sequence of between 16 and 30 nucleotides, wherein the nucleotide sequence is substantially identical to consecutive nucleotides of an mRNA encoding a polypeptide of SEQ ID NO: 2, and wherein the cell comprising the RNA polynucleotide has decreased MscCa activity, decreased motility, decrease invasiveness, or a combination thereof, when compared to a control cell that does not comprise the RNA polynucleotide.

32. A method for treating cancer comprising:

administering to a subject having cancer an effective amount of an RNA polynucleotide, wherein the polynucleotide comprises a sense strand and an antisense strand, wherein the sense strand comprises a nucleotide sequence of between 16 and 30 nucleotides, wherein the nucleotide sequence is substantially identical to consecutive nucleotides of an mRNA encoding a polypeptide of SEQ ID NO: 2, and wherein a symptom of the cancer is decreased.

33. A method for decreasing metastasis of a cancer cell comprising:

administering to a subject at risk of developing cancer an effective amount of an RNA polynucleotide, wherein the polynucleotide comprises a sense strand and an antisense strand, wherein the sense strand comprises a nucleotide sequence of between 16 and 30 nucleotides, and wherein the nucleotide sequence is substantially identical to consecutive nucleotides of an mRNA encoding a polypeptide of SEQ ID NO: 2.

34. A method for decreasing a symptom associated with cancer comprising:

administering to a subject having cancer an effective amount of an RNA polynucleotide, wherein the polynucleotide comprises a sense strand and an antisense strand, wherein the sense strand comprises a nucleotide sequence of between 16 and 30 nucleotides, wherein the nucleotide sequence is substantially identical to consecutive nucleotides of an mRNA encoding a polypeptide of SEQ ID NO: 2.

\* \* \* \* \*

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## APPLICATION DATA SHEET

## APPLICATION INFORMATION

Application Type:: REGULAR  
Subject Matter:: UTILITY  
CD-ROM or CD-R?: NONE  
Title:: MECHANOSENSITIVE ION CHANNELS  
AND METHODS OF USE  
Attorney Docket Number:: 265.00450101  
Small Entity?: YES

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Country of Mailing Address:: US  
Postal or Zip Code of Mailing Address:: 77550

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10. The method of claim 1 wherein the treated cell has increased apoptosis compared to the control cell.
11. An agent identified by the method of claim 1.
12. A method for identifying an agent that decreases a phenotype of a cell comprising:
  - contacting a cell expressing an MscCa channel with a candidate agent to yield a treated cell; and
  - comparing the phenotype of the treated cell with the phenotype of a control cell not contacted with the candidate agent, wherein the phenotype is selected from the group of motility, invasiveness, proliferation, and a combination thereof, and wherein a decreased phenotype for the treated cell indicates the candidate agent decreases the phenotype.
13. The method of claim 12 wherein the candidate agent causes activity of an MscCa channel of the treated cell to decrease.
14. The method of claim 12 wherein the MscCa channel comprises a polypeptide comprising an amino acid sequence of at least 90% identity to SEQ ID NO: 2, wherein the polypeptide has MscCa activity.
15. The method of claim 14 wherein the MscCa channel comprises a polypeptide comprising SEQ ID NO: 2.
16. The method of claim 12 wherein the cell is a tumor cell.
17. The method of claim 12 wherein the cell is a human prostate tumor cell line.
18. The method of claim 17 wherein the human prostate tumor cell line is ATCC CRL-1435.
19. An agent identified by the method of claim 12.

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20. A method for treating cancer comprising:  
administering to a subject having cancer an effective amount of a composition comprising an agent that decreases activity of a mechanosensitive ion channel present on a cancer cell, wherein a symptom of the cancer is decreased.
21. A method for decreasing metastasis of a cancer cell comprising:  
administering to a subject at risk of developing cancer an effective amount of a composition comprising an agent that decreases activity of a mechanosensitive ion channel.
22. A method for decreasing a symptom associated with cancer comprising:  
administering to a subject having cancer an effective amount of a composition comprising an agent that decreases activity of a mechanosensitive ion channel.
23. The method of claim 20, 21, or 22 wherein the mechanosensitive ion channel is a mechanosensitive  $\text{Ca}^{2+}$ -permeable (MscCa) channel.
24. The method of claim 20, 21, or 22 wherein the agent is a polypeptide comprising an amino acid sequence comprising at least 90% identity to SEQ ID NO:1 or to SEQ ID NO:7.
25. The method of claim 24 wherein the agent is a polypeptide comprising SEQ ID NO:1 or SEQ ID NO:7.
26. The method of claim 23 wherein the agent is an antibody that specifically binds an MscCa polypeptide.
27. The method of claim 26 wherein the antibody binds to an epitope present on SEQ ID NO:5 or SEQ ID NO:6.



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28. The method of claim 23 wherein the MscCa channel comprises an MscCa polypeptide, and wherein the agent is a polynucleotide that decreases expression of the MscCa polypeptide.
29. The method of claim 20, 21, or 22 wherein the cancer is prostate cancer, breast cancer, colon cancer, lung cancer, bladder cancer, ovary cancer, pancreas cancer, or skin cancer.
30. The method of claim 23 wherein the agent decreases activity of an MscCa channel comprising a polypeptide comprising SEQ ID NO: 2.
31. A method for inhibiting expression of an MscCa polypeptide comprising:  
administering into a cell an effective amount of an RNA polynucleotide, wherein the polynucleotide comprises a sense strand and an antisense strand, wherein the sense strand comprises a nucleotide sequence of between 16 and 30 nucleotides, wherein the nucleotide sequence is substantially identical to consecutive nucleotides of an mRNA encoding a polypeptide of SEQ ID NO:2, and wherein the cell comprising the RNA polynucleotide has decreased MscCa activity, decreased motility, decreased invasiveness, or a combination thereof, when compared to a control cell that does not comprise the RNA polynucleotide.
32. A method for treating cancer comprising:  
administering to a subject having cancer an effective amount of an RNA polynucleotide, wherein the polynucleotide comprises a sense strand and an antisense strand, wherein the sense strand comprises a nucleotide sequence of between 16 and 30 nucleotides, wherein the nucleotide sequence is substantially identical to consecutive nucleotides of an mRNA encoding a polypeptide of SEQ ID NO:2, and wherein a symptom of the cancer is decreased.
33. A method for decreasing metastasis of a cancer cell comprising:  
administering to a subject at risk of developing cancer an effective amount of an RNA polynucleotide, wherein the polynucleotide comprises a sense strand